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Serum prealbumin levels and their association with serum albumin, calcium, magnesium, and phosphorus concentrations

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ABSTRACT

Aims: Prealbumin is a specific and sensitive marker of nutritional conditions. The aim of our study was to investigate the relationship between serum prealbumin concentrations and serum albumin, magnesium, phosphorus and calcium levels.

Methods: A total of 200 patients, 100 male and 100 female, aged 18-65 years, who applied to the Ankara Etlik City Hospital Internal Medicine Polyclinic between January 2023 and June 2023, were included in our study. The patients' prealbumin, albumin, calcium, magnesium, phosphorus, creatinine, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and complete blood count parameters (hemoglobin, white blood cell (WBC), platelet (PLT)) results were evaluated.

Results: The median prealbumin of female subjects was 0.50 g/L (0.1-1.0), while the median prealbumin of male subjects was 0.40 g/L (0.1-1.0). There was no statistically significant difference between the groups ($p>0.05$). There is a direct positive between prealbumin concentration and calcium (r: 0.75; $p<0.001$), hemoglobin (r: 0.46; $p<0.001$), LDL (r: 0.50; $p<0.001$) and HDL (r: 0.63; $p<0.001$) concentrations and an negative correlation between magnesium (r: -0.16; p:0.02) and PLT (r: -0.31; $p<0.001$). Logistic regression analysis was performed to determine the independent variables affecting prealbumin concentration. The independent variables included in the model were HDL, LDL, body mass index (BMI), creatinine, WBC, phosphorus, age, magnesium, albumin, PLT, hemoglobin, and calcium. The Nagelgerke R2 square value of the model was 0.73 and the p value of the model in ANOVA analysis was calculated as <0.001. A regression formula for prealbumin concentrations was found: Prealbumin concentration = -0.609 + (Age × -0.002) + (BMI × 0.001) + (Ca × 0.63) + (Mg × -0.020) + (P × -0.002) + (Creatinine × 0.034) + (Hb × 0.016) + (WBC × -0.004) + (HDL × 0.001) + (LDL × 0.004).

Conclusion: We think that the findings of our study will be useful in elucidating the relationship between serum prealbumin and albumin levels, which are important indicators of dietary protein intake, and serum mineral concentrations. Our study is an article that presents a regression formula for prealbumin. The diagnostic and prognostic importance of prealbumin can be further elucidated by recruiting special and larger patient groups.

Keywords: Prealbumin, albumin, calcium, magnesium, phosphorus

INTRODUCTION

Prealbumin is an important protein mainly found in blood and has a molecular weight of 55 kDa. Although most of it is synthesised in hepatocytes, a very small amount originates from tissues such as pancreas.[1] This protein is also known and named as transthyretin because of its thyroid hormones and vitamin A binding properties.[2] Prealbumin is a specific and sensitive marker of nutritional conditions.[3,4] The half-life of prealbumin is approximately 60 hours. It is even more valuable in showing short-term nutritional differences in the human body due to this short half-life.[5] In individuals over 18 years of age, the reference range for this protein is 0.2-0.4 g/L.[4] Prealbumin is also a negative acute phase reactant. Therefore, laboratory data of these protein concentrations should be carefully evaluated. If there are other conditions accompanying the patient, it may lead to erroneous interpretations. For example, serum prealbumin level may decrease significantly in severe infections, inflammatory conditions and traumatic conditions.[6] Since this molecule undergoes various post translational modifications, its association with many important diseases such as Alzheimer's disease and familial amyloidic neuropathy has been shown.[7,8] In addition, there are studies reporting the association of prealbumin with the prognosis of many diseases such as COVID-19 mortality, liver transplantation, acute pancreatitis, gastric cancer, hepatocellular carcinoma and breast cancer.[9-16]

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Serum albumin levels are also related with inflammatory processes and nutritional conditions.[17] Just like prealbumin, albumin is a negative acute phase reactant and its serum levels decrease in the presence of inflammation and inadequate nutrition.[18] Albumin has a longer half-life compared to prealbumin and is synthesised more slowly in the liver.[5,19]

Calcium (Ca), phosphorus (P) and magnesium (Mg) play important roles in the growth and metabolism of many tissues including bone.[20] The extracellular fraction of calcium binds especially to serum albumin.[21] However, it has long been established that a part of calcium also binds to prealbumin with an affinity similar to albumin.[22] Since calcium binds to both albumin and the nutritional marker prealbumin and its levels change with nutritional status, an important relationship network is in question. Magnesium and phosphorus, like calcium, are essential for bone mineralisation and many cellular functions.[23] Therefore, all proteins in question have a close relationship with each other both functionally and quantitatively.

After all the reasons and mechanisms described above, we thought that prealbumin concentrations may be related with serum albumin, magnesium, phosphorus and calcium levels and that we may obtain new data or formulae. In summary, the aim of our study was to investigate the possible relationship between serum prealbumin concentrations and serum albumin, magnesium, phosphorus and calcium levels.

METHODS

The study was carried out with the permission of Ankara Bilkent City Hospital No: 1 Clinical Researches Ethics Committee (Date: 30.11.2022, Decision Number: E1/3061/2022). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Study Population

This is a retrospective observational study a total of 200 patients, 100 male and 100 female, aged 18-65 years, who applied to the Ankara Etlik City Hospital Internal Medicine Polyclinic between January 2023 and June 2023, were included in our study. Individuals whose serum albumin, prealbumin, magnesium, phosphorus and calcium parameters, as well as routine biochemistry and complete blood counts were reported simultaneously in the central biochemistry laboratory were included in our study. The inclusion and exclusion criteria are as follows.

Inclusion criteria: Age between 18 and 65 years, no known psychotic illness, no diagnosis of alcoholism, no chronic inflammatory liver disease, no chronic drug use, no history of malignant neoplasia, and liver function tests (alanine aminotransferase (ALT), aspartate) Aminotransferase (AST), gamma-glutamyl transferase (GGT), prothrombin time (PT), direct bilirubin, total bilirubin) within normal limits.

Exclusion criteria: People who did not have the above-mentioned characteristics were excluded from our study.

Demographic information and laboratory results of the patients were obtained electronically through the laboratory information system (LIS). According to the World Health Organisation recommendations, the study groups were grouped according to BMI levels as underweight (<18.5), normal (18.5-24.9), pre-obesity (25.0-29.9), obesity class I (30.0-34.9), obesity class II (35.0-39.9) and obesity class III (≥40.0).[24] Ankara Etlik City Hospital coordinator chief physician permission was also obtained for the use of patient data. Since the ethics committee was not yet ready when our hospital was newly established, ethics committee permission was obtained from the Ethics Committee of Ankara City Hospital.

Laboratory Analysis

The patients' prealbumin, albumin, calcium, magnesium, phosphorus, creatinine, low-density lipoprotein (LDL), high-density lipoprotein (HDL), PT and complete blood count parameters (hemoglobin, white blood cell (WBC), platelet (PLT) results were evaluated. The routine operation of our laboratory when performing the tests whose results we evaluated in our study is as follows. Venous blood and whole blood samples are taken from these individuals after 10-12 hours of fasting. 8-10 mL of venous blood is collected in a tube containing clot activator and gel, then waited for 20-30 minutes and centrifuged at 1500-2000 g for 10 minutes to obtain a serum sample. Biochemical parameters are measured using these serum samples and analysed on a Roche Cobas c 702 (Roche Diagnostics GmbH, Mannheim, Germany) autoanalyzer. These autoanalysers measure prealbumin by immunoturbidimetric method, albumin by colorimetric method (using bromocresol green), calcium, magnesium and phosphorus by colorimetric method, ALT and AST by photomeric method and GGT, LDL and HDL by colorimetric enzyme method. PT is measured with the cobas t 711 (Roche Diagnostics GmbH, Mannheim, Germany) autoanalyser. For complete blood count, a whole blood sample is collected in a purple capped tube containing K-EDTA and analysed on a Sysmex XN1000 (Sysmex corp. Kobe, Japan). In this device, hemoglobin is measured by photometric method, platelets by optical scattering and impedance method and WBC by fluorescence dyed light scattering method. In addition to these parameters, demographic information such as age and gender were obtained from LIS.

Statistical Analysis

Data were analysed using the statistical package programme Analyze-It for Microsoft Excel 5.80.2. The suitability of the data for normal distribution was determined by Shapiro-Wilk test. Categorical variables were shown as (n,%), data with and without normal distribution were expressed as mean SD and median (min-max), respectively. Comparison of prealbumin and categorical variables was evaluated by t test if the data were normally distributed and by Mann-Whitney U test or Kruskal-Wallis test if the data were not normally distributed. The relationship between prealbumin and laboratory parameters was evaluated by Pearson correlation test. Independent risk factors affecting prealbumin level were investigated by linear regression test. Statistical significance level was stated as p<0.05.

RESULTS

Demographic and laboratory characteristics of the study group are presented in Table 1. The median prealbumin of female subjects was 0.50 g/L (0.1-1.0), while the median prealbumin of male subjects was 0.40 g/L (0.1-1.0). There was no statistically significant difference between the groups (p=0.53; evaluated by Mann-Whitney U test). According to BMI levels, the subjects were grouped as underweight, normal, pre-obesity, obesity class I, obesity class II and obesity class III. The median prealbumin values of the groups were 0.5 g/L (0.1-0.9); 0.4 g/L (0.1-1.0); 0.4 g/L (0.1-1.0); 0.4 g/L (0.1-1.0); 0.5 g/L (0.1-0.9) and 0.4 g/L (0.1-1.0), respectively. There was no statistically significant difference between the groups (p=0.54). Table 2 shows the correlation relationship between prealbumin and laboratory parameters. There is a direct positive between prealbumin concentration and calcium (r: 0.75; p<0.001), hemoglobin (r: 0.46; p<0.001), LDL (r: 0.50; p<0.001) and HDL (r: 0.63; p<0.001) concentrations and an negative correlation between magnesium (r: -0.16; p:0.02) and PLT (r: -0.31; p<0.001).

Table 1. Demographic and laboratory characteristics of the study group

Parameters		
Gender (n.%)	Female	100 (50.0%)
	Male	100 (50.0%)
Age (year)		41.0 (18.0-65.0)
BMI (kg/m2)		27.8 (14.1-40.6)
Prealbumin (g/L)		0.5 (0.1-1.0)
Albumin (g/L)		44.0 (20.0-64.0)
Calcium (mg/dl)		10.1 ±1.8
Magnesium (mg/dl)		2.70 (0.9-4.30)
Phosphorus (mg/dl)		4.6 (1.6-6.7)
Creatinin (mg/dl)		1.0 (0.5-1.4)
Hemoglobin (g/dl)		14.0 (9.2-18.0)
WBC (cell/µl)		8.1 (2.4-15.4)
PLT (cell/µl)		320.0 (132.0-597.0)
LDL (mg/dl)		105.0 (49.0-197.0)
HDL (mg/dl)		53.0 (20.0-82.0)

Categorical variables were shown as (n.%), data with and without normal distribution were expressed as mean SD and median (min-max), respectively. WBC: White blood cell; PLT: Platelet; LDL: Low-density lipoprotein; HDL: High-density lipoprotein

Table 2. Correlation relationship between prealbumin and laboratory parameters

Variable		Prealbumin	Albumin	Calcium	Magnesium	Phosporus	Creatinin	Hemoglobin	WBC	PLT	LDL	HDL
Prealbumin	Pearson	(-)										
	p value	(-)										
Albumin	Pearson	-0.04	(-)									
	p value	0.56	(-)									
Calcium	Pearson	0.75	0.10	(-)								
	p value	<0.001	0.13	(-)								
Magnesium	Pearson	-0.16	-0.40	-0.06	(-)							
	p value	0.02	0.51	0.34	(-)							
Phosporus	Pearson	0.05	0.05	0.08	-0.02	(-)						
	p value	0.42	0.50	0.21	0.74	(-)						
Creatinin	Pearson	0.05	0.04	0.02	0.02	0.06	(-)					
	p	0.47	0.54	0.76	0.74	0.29	(-)					
Hemoglobin	Pearson	0.46	-0.03	0.36	0.02	0.03	-0.06	(-)				
	p	<0.001	0.64	<0.001	0.73	0.04	0.13	(-)				
WBC	Pearson	-0.03	-0.01	0.01	-0.01	0.06	0.01	-0.07	(-)			
	p	0.67	0.11	0.84	0.09	0.39	0.90	0.19	(-)			
PLT	Pearson	-0.31	0.04	-0.25	0.06	-0.05	0.12	-0.21	-0.08	(-)		
	p	<0.001	0.53	<0.001	0.33	0.58	0.34	0.76	<0.001	(-)		
LDL	Pearson	0.50	-0.06	0.39	-0.07	0.10	0.09	0.28	0.04	0.04	(-)	
	p	<0.001	0.33	<0.001	0.09	0.36	0.81	0.31	<0.001	0.56	(-)	
HDL	Pearson	0.63	-0.01	0.50	-0.01	0.00	0.02	0.32	0.01	-0.26	0.31	(-)
	p	<0.001	0.80	<0.001	0.33	0.46	0.06	<0.001	0.21	<0.001	<0.001	(-)

WBC: White blood cell; PLT: Platelet; LDL: Low-density lipoprotein; HDL: High-density lipoprotein. Bolded numbers are the results considered statistically significant (p<0.05).

Logistic regression analysis was performed to determine the independent variables affecting prealbumin concentration. The independent variables included in the model were HDL, LDL, BMI, creatinine, WBC, phosphorus, age, magnesium, albumin, PLT, hemoglobin, and calcium. The Nagelgerke R2 square value of the model was 0.73 and the p value of the model in ANOVA analysis was calculated as <0.001. A summary of the model is presented in Table 3. Age, calcium, magnesium, hemoglobin, HDL and LDL cholesterol are the values that affect prealbumin concentration independently of other variables. The regression equation is shown in Formula 1.

Formula 1: Prealbumin concentration = -0.609 + (Age × -0.002) + (BMI × 0.001) + (Ca × 0.63) + (Mg × -0.020) + (P × -0.002) + (Creatinine × 0.034) + (Hb × 0.016) + (WBC × -0.004) + (HDL × 0.001) + (LDL × 0.004)

Table 3. Independent variables affecting prealbumin concentration

Variable	B	Sig	95% CI
Constant	-0.609	.000	(-.836 ; -.382)
Age	-0.002	.027	(-.003; .000)
Albumin	.000	.777	(-.001; .002)
Body mass index	.001	.616	(-.002; .003)
Calcium	.063	.000	(.051; .760)
Magnesium	-.020	.032	(-.038; -.002)
Phosporus	-.002	.720	(-.015; .020)
Creatinin	.034	.332	(-.035; .102)
Hemoglobin	.016	.001	(.007; .025)
WBC	-.004	.121	(-.009; .001)
PLT	.000	.023	(.000; .000)
HDL	.001	.000	(.001; .002)
LDL	.004	.000	(.003; .006)

WBC: White blood cell; PLT: Platelet; LDL: Low-density lipoprotein; HDL: High-density lipoprotein. CI: Confidence Interval, Bolded numbers are the results considered statistically significant (p<0.05).

DISCUSSION

Prealbumin, also known as transthyretin, is a specific marker of nutritional status and is a protein associated with the pathogenesis and prognosis of many diseases. The first striking finding was the negative correlation between magnesium and platelets and prealbumin. A negative correlation between prealbumin and PLT may be due to reactive thrombocytosis in malnutrition, just as in iron deficiency anaemia. However, the negative correlation between prealbumin and magnesium contrary to the literature was an unexpected result for us.[25,26] Changes in nutritional conditions may cause significant changes in free magnesium concentrations by affecting prealbumin and albumin levels. Since approximately one third of serum magnesium is bound to proteins, especially albumin, molecular interactions, which are not yet known and may be revealed in further research, may have produced this negative correlation.[27] In addition, we showed that serum prealbumin concentrations were positively correlated with calcium, LDL, HDL and hemoglobin levels. Our study also provides a specific formula for estimating serum prealbumin levels. In this formula, serum prealbumin level is calculated by using the patient's age, hemoglobin, LDL, HDL, magnesium, calcium, and age parameters. Our aim in searching for a regression formula is to predict the prealbumin concentration with related parameters in laboratories where measurement of prealbumin concentration cannot be performed.

In a study conducted with hemodialysis patients, Chertow et al.[28] reported that serum prealbumin values were directly correlated with albumin values. In addition, in this study, prealbumin was shown to have prognostic importance in hemodialysis patients. The superior aspects of our study are the correlation of serum prealbumin concentrations not only with albumin but also with parameters such as calcium, magnesium, phosphorus, LDL, HDL and hemoglobin and the development of a special formula to predict prealbumin levels. However, the lack of a specific disease group and the lack of investigation of prognostic significance are the negative aspects of our study.

In a study conducted in 2017 on 664 women with osteoporosis in China, serum prealbumin levels were shown to be directly correlated with bone mineral density (BMD).[29] In this study, it was found that serum prealbumin concentrations decreased as BMD decreased. Although a specific patient population was selected in this study, the fact that the correlation of BMD and prealbumin with molecules that play important roles in bone mineralisation such as serum calcium, magnesium and phosphorus was not investigated was a negative factor compared to our study.

The study conducted by Xiu et al.[30] in 2019 in osteoporotic patients with type 2 diabetes mellitus showed that prealbumin levels were higher in those without osteoporosis and that low prealbumin levels increased the risk of osteoporosis. Therefore, this study re-emphasised that a poor nutritional status increases the risk of osteoporosis. The selection of a specific patient group as in other studies is a superior feature of this study, but it also has negative aspects compared to our study. These negative aspects are that the correlation between prealbumin and parameters such as albumin, calcium, magnesium, phosphorus, hemoglobin, HDL and LDL was not investigated.

Handcox et al.[31] performed a retrospective observational study looking at serum prealbumin, albumin, magnesium and phosphorus levels in orthopaedic trauma patients. In this study, it was reported that

orthopaedic traumas were experienced more frequently and wound complications were observed more frequently in patients with low prealbumin levels. This study could not show a correlation between magnesium and phosphorus and these pathologies. In our study, the correlation of prealbumin with calcium and magnesium was shown.

Study Limitations

Our study had limitations such as small population size, lack of a specific disease group, lack of power analysis, being a retrospective study, and multifactorial and variable prealbumin metabolism. In addition, it should not be forgotten that external validation of the formula we have put forward should be done.

Strengths of the study: The strengths of our study include an extensive and up-to-date review of the literature on the subject, highlighting many possible relationships with prealbumin, calculating the correlation with many parameters, introducing a new formula that can be used in hospitals where prealbumin cannot be measured and effective statistical analysis.

CONCLUSION

In our study, we showed that serum prealbumin concentrations were positively correlated with calcium, LDL, HDL and hemoglobin levels and negatively correlated with magnesium and platelet levels. Although some of our findings differ from a few studies in the literature, this article may be a guide for new and further studies. We think that the findings of our study will be useful in elucidating the relationship between serum prealbumin and albumin levels, which are important indicators of dietary protein intake, and serum mineral concentrations. The fact that there are not many studies on this subject in the literature makes our study more valuable. Multicentre and long-term studies may be useful to generalise our results. Our study is the first manuscript to present a regression formula for prealbumin. The diagnostic and prognostic importance of prealbumin can be demonstrated in studies with different disease groups and groups of completely healthy volunteers.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Bilkent City Hospital No: 1 Clinical Researches Ethics Committee (Date: 30.11.2022; Decision Number: E1/3061/2022).

Informed Consent: Because the study was designed retrospectively, no written informed consent from was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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